

### **REMARKS**

Applicants wish to thank Examiner Bernhardt for discussing the pending claims in a telephone conference on May 16 with Applicants' attorney Nicholas P. Triano III.

Claims 13-17, 19-29, 38, 40, 44, 50, 52, 57-58, 68-72, 84-85 and 87-97 have been cancelled without prejudice or disclaimer. Claims 1-3, 5, 8-10, 12, 18, 30-37, 39, 41-43, 45-49, 51, 53-56, 59, 60, 62-64, 66-67, 73-83 and 86 have been amended. Claims 21-29, 40, 44, 50, 84-85 and 89-97 were originally subjected to restriction and were withdrawn, but are formally canceled herein without prejudice or disclaimer. Claim 98 is new. *Accordingly, claims 1-12, 18, 30-37, 39, 41-43, 45-49, 51, 53-56, 59-67, 73-83, 86 and 98 are in the case.*

Applicants' attorney wishes to inform the Office that he has left Mintz Levin Cohn Ferris Glovsky and Popeo PC and is now Counsel at Goodwin Procter LLP, Exchange Place, 53 State Street, Boston, MA 02109. A Revocation Of Prior Powers And New Power Of Attorney document was filed in the present case on March 27, 2006, a copy of which is enclosed for the Examiner's convenience. The Office is requested to mail all subsequent papers to the attention of the Patent Administrator, Goodwin Procter LLP, Exchange Place, 53 State Street, Boston, MA 02109.

### **Objections**

The Examiner objected to the Abstract as it was said to not depict the structural makeup of Applicants' invention. The Abstract as been amended to also include the structures of Formula II, but Applicants respectfully submit that if the Examiner wishes to include chemical structures in the Abstract, that it would perhaps be better to amend the Abstract prior to issuance.

### **Rejection(s) under 35 U.S.C. § 112**

Claims 1-20, 30-37, 39, 41-43, 45-49, 51, 53-83, and 86-88 were rejected under 35 U.S.C. §112, second paragraph as indefinite for failing to particularly point out and distinctly claim the subject matter Applicants regard as the invention. Applicants' response will correspond to the points raised by the Examiner in the order presented in the Office Action:

1. Applicants have amended claims 1 and 56 to specify that (as the Examiner correctly points out)  $R_2$  may be nitro (*i.e.*,  $-NR_4R_5$ , where  $R_4$  and  $R_5$  are both oxygen).
2. Claims 1 and 56 have been amended to clarify the definition of  $R_6$ . No new matter is added.
3. Claims 1 and 56 have been amended not to acquiesce in the rejection, but in order to focus the claims on certain embodiments of the invention, *i.e.*, wherein Y represents a) an amino or amino(lower alkyl) group or b) a piperidinyl ring; and the language reciting “the atoms denoted by the dotted line bond...” has been deleted. Example compounds of a) in the specification include Example 12 ( $n=4$  in this case) and Example 27; and example compounds of b) in the specification include Example 20 (where  $n=1$  in this case).
4. Applicants have amended the claims throughout not to acquiesce in the rejection, but to advance prosecution and specify that the claims relate to the compounds of the invention and/or their pharmaceutically acceptable salt(s).
5. The end of claim 1 has been amended to clarify the claim and moot the rejection.
6. Claim 2 has been amended for clarity. No new matter is added.
7. “Alkoxy” in claims 7 and 61 now has antecedent basis in claims 1 and 56, respectively.
8. Claims 8 and 62 have been amended to clarify the definition of the recited cycloalkyl ring. No new matter is added.
9. Applicants traverse; the three cycloalkyl groups are preferred cycloalkyl groups within the scope of Applicants’ invention, and are thus within the scope of the definition of cycloalkyl; *see, e.g.*, the specification at page 4, lines 19-20.
10. The rejection is mooted by Applicants’ cancellation of claims 13-17 and 68-72 without prejudice or disclaimer.

11. The rejection is mooted by Applicants' amendment of claims 18 and 86, and cancellation of claims 19-20 and 87-88. The amendments are respectfully believed to address the Examiner's concerns.
12. Claims 30-37, 49, 41-43, 45-49, 51, 53-55 and 73-83 have been amended to clarify that the claims are directed to the recited compound or its pharmaceutically acceptable salt (which claim would naturally cover a composition containing the recited subject matter.)
13. Claims 47 and 51 have been amended to correct the compound name, *i.e.*, make it consistent with its structure as depicted in the specification. No new matter is added.

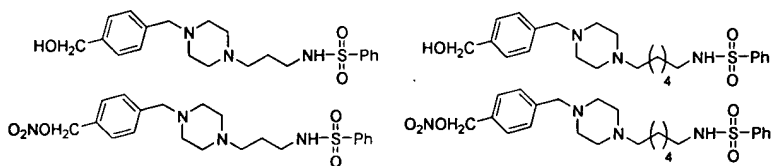
Claims 1-20, 56-72, and 86-88 were rejected under 35 U.S.C. §112, first paragraph as indefinite for failing to comply with the enablement requirement. Briefly, it was said that

“the claims contain subject matter not described in the specification in such as way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Scope of piperazines covered by the generic claims is not adequately enabled. From a reading of the specification (pages 1-15) terms such as alkyl, aryl, cycloalkyl, alkenyl, acyl, etc. are not given their normal meanings but also include a plethora of substituents thereon. “Aryl” includes in addition to aromatic carbocyclics, 5- and 6- membered heteroaromatics that can be further fused. Additionally, there can be “conjugated” cyclic rings in R<sub>2</sub> and R<sub>3</sub> which appear to include fused “Z” rings. Also rings can form on nitrogen attached to sulfonyl. Compounds made and tested do not represent such a scope as they are phenyl piperazines having substituents such as those recited in claim 2 corresponding to **unsubstituted** alkyls and cycloalkyls with R<sub>1</sub> being predominantly tolyl or to a lesser extent cyclohexylmethyl and unsubstituted lower alkyl. The only example of a ring being formed at C—N is piperidino. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 21564.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art.”

**Rejection(s) under 35 U.S.C. § 102**

Claims 1, 2, 7, 8, 12-20, 56, 61, 62, 66, 68-72 and 86-88 were rejected under 35 U.S.C. §102(b) as anticipated by JP 09202764 to Uchida (Chemical Abstract provided) ("Uchida"). The Examiner argued that Uchida describes compounds within the scope of the present application because the Applicants' definition of "alkyl" or "lower alkyl" includes substituted derivatives. *See*, Office Action at page 11. Applicants traverse the rejection as it applies to the pending claims as amended herein.

Uchida discloses compounds substituted with  $-\text{CH}_2\text{OH}$  and  $-\text{CH}_2\text{ONO}_2$  on the aryl group attached to the piperazine ring as shown below.



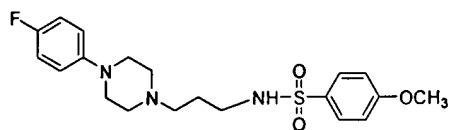
As amended, the claims have been clarified to recite that  $\text{R}_2$  and  $\text{R}_3$  independently are hydrogen, nitro, lower alkoxy, or  $-\text{NR}_4\text{R}_5$  (provided that  $\text{R}_2$  and  $\text{R}_3$  are not both hydrogen.) Furthermore, the presently amended claims do not feature a phenyl moiety bonded to the sulfonyl group. As such, Applicants submit that Uchida does not anticipate the pending claims 1, 2, 7, 8, 12, 18, 56, 61, 62, 66, and 86-88, as amended herein, and respectfully request that this rejection be withdrawn.

Claims 1, 2, 7, 8, 11, 13-20, 56, 61, 62, 65, 68-72 and 86-88 were rejected under 35 U.S.C. §102(b) as anticipated by EP 0089089 ("Van Dalen"). The Examiner states that Van Dalen describes a compound (Example III<sup>1</sup>) within the scope of the claims, because the trifluoromethyl substituent on the phenyl ring of the compound is "within the ambit of substituted alkyl and substituted lower alkyl as defined by Applicants' specification." Applicants traverse the rejection as it applies to the pending claims as amended herein. The claims have

been amended to state that R<sub>2</sub> and R<sub>3</sub> do not include trihalomethyl. As such, Van Dalen does not anticipate the rejected pending claims as amended herein, and Applicants respectfully request that this rejection be withdrawn.

The Examiner rejected claims 1, 2, 7, 8, and 11-20 under 35 U.S.C. 102(b) as being anticipated by EP 0661266 ("Aoki"). The Examiner asserts that Aoki describes a compound (Example 24 on p. 44) within the scope of the present invention. Applicants traverse the rejection as it applies to the pending claims as amended herein.

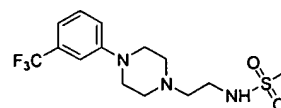
Aoki discloses N-(3-(4-fluorophenyl)piperazinyl)propyl)-4-methoxybenzene sulfonamide,



. Claim 1 has been amended to advance prosecution and towards a particular embodiment wherein R<sub>1</sub> does not include an aryl substituent on the sulfonyl group. As such, Aoki does not anticipate pending claims 1, 2, 7, 8, 11-12, and 18, as amended. Applicants respectfully request withdrawal of the rejection.

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<sup>1</sup> N-[2-(4-(3-trifluoromethyl)phenyl)-1-piperazinyl)ethyl)methanesulfonamide,



**Rejection(s) under 35 U.S.C. § 103**

The Examiner rejected claims 3-6, 9-10, 56-66, 68-72 and 86-88 under 35 U.S.C. 103(a) as unpatentable over Aoki. The Examiner submits that one of ordinary skill in the art would find it obvious to modify the Aoki compound of Example 24 noted above by, *e.g.*, replacing the methoxy group on phenylsulfonyl with groups such as halo. Applicants traverse the rejection as it applies to the pending claims as amended herein.

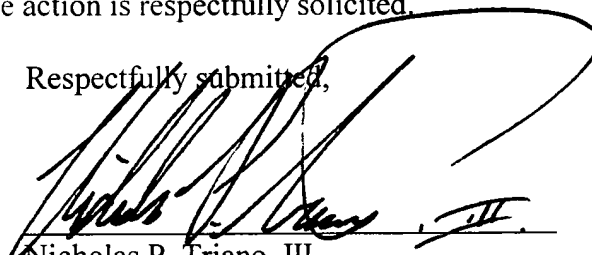
As noted above, Claim 1 has been amended to advance prosecution, and towards a particular embodiment wherein R<sub>1</sub> does not include an aryl substituent on the sulfonyl group. As such, one of ordinary skill in the art would not reasonably find claims 3-6, 9-10, 56-66, 68-72 and 86-88, as amended, obvious over Aoki. Applicants respectfully request withdrawal of the rejection.

Applicants also appreciate the Examiner's recognition of the patentability of the independent species claims, which claims should proceed to allowance in view of the amendments and arguments made herein addressing the rejections of the other claims.

**CONCLUSION**

In view of the foregoing, Applicants respectfully request that the foregoing rejections be reconsidered and withdrawn. The Examiner is invited to contact the undersigned with any questions about this submission. Early favorable action is respectfully solicited.

Respectfully submitted,



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